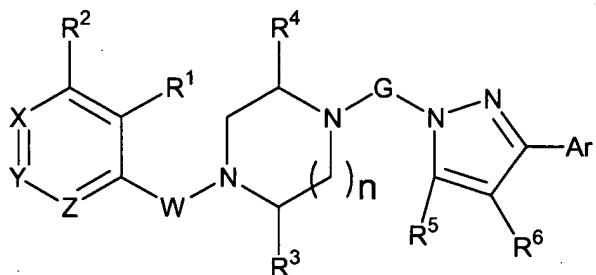


## REMARKS

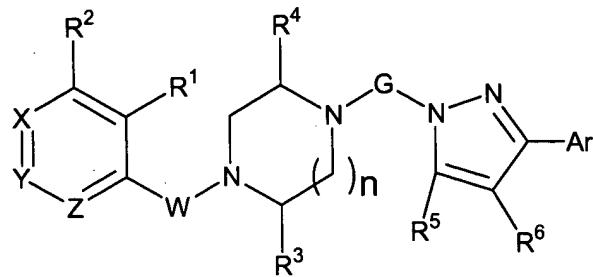
Applicants thank the Examiner for including in the Office Action the previously filed PTO1449 forms, now with the references therein of record, and also for the consideration given to the response submitted with Amendment and Response "B" on May 28, 2004, which is understood as having been entered in the records of the present application.

Presently pending claims 1-8 of co-pending application US 09/947,041 (hereinafter the "'041 Application") recite methods that comprise administering a composition that comprises a compound recited in claims 1-8 therein. Such claims 1-8 depend, directly or through other depending intervening claims, from independent claim 1 therein. Such claim 1 recites, *inter alia*, a compound of formula



in which R<sup>5</sup> and R<sup>6</sup> "can be taken together to form an optionally substituted 5- to 7-membered heterocyclic ring, a 5-membered carbocyclic ring, or a 7-membered carbocyclic ring, which ring may be unsaturated or aromatic, and may be optionally substituted with ...". The '041 Application, Amendment and Response "C", filed December 20, 2004. (A list of the presently pending claims in the '041 Application is provided in Attachment "A").

The claims in the present application recite subject matter that refers, directly or through other depending intervening claims, to the following compound:



in which  $R^5$  and  $R^6$  are “taken together to form pyridinyl or 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...”.

It follows from at least the quoted recitations of portions of the claims in the '041 Application and portions of the claims in the present application, that such claims recite different subject matter.

Regarding the recitation of a subgenus of reference claims, note that claims that recited overlapping subject matter in the form of a genus of the compounds in pending claims were not considered support for a nonstatutory double patenting rejection because the genus and sub-genus recited therein were patentably distinct from each other. *See, e.g., In re Sarett*, 327 F.2d 1005 (C.C.P.A. 1964) (reversing all the rejections by the US PTO Board of Patent Appeals and Interferences that had been predicated on nonstatutory double patenting, and holding that the claims in a pending patent application that specifically recited a “pyridine-chromium trioxide complex” as an oxidizing agent were patentably distinct from the claims in an issued patent that generically recited “an oxidizing agent”).

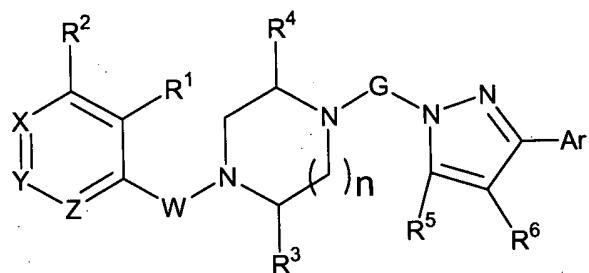
Applicants respectfully note that

[o]ne significant difference [between a double patenting rejection and rejections based on prior art] is that a double patenting rejection must rely on a comparison with the claims in an issued or to be issued patent, whereas an obviousness rejection based on the same patent under 35 U.S.C. [§§] 102(e)/103(a) relies on a comparison with what is disclosed (whether or not claimed) in the same issued or to be issued patent. In a 35 U.S.C. [§§] 102(e)/103(a) rejection over a prior art patent, the reference patent is available for all that it fairly discloses to one of ordinary skill in the art, regardless of what is claimed. (Citation omitted).

M.P.E.P. § 804.III, p. 800-29, 8<sup>th</sup> ed. (Aug. 2001). The comparison of the pending claims with claims 43-45 in the '122 Application reveals that they recite different subject matter and that the pending claims are not obvious variations of the claims in the '041 Application.

Applicants respectfully submit that the pending claims may not be rejected under the nonstatutory double patenting doctrine in view of claims of the '041 Application, and consequently request the removal of these rejections.

Claims of co-pending application US 10/075,673 (hereinafter the "'673 Application") recite methods that comprise administering a composition that comprises a compound recited, directly or by incorporation from one or more dependent claims, in independent claim 1 therein. Such claim 1 recites, *inter alia*, a compound of formula



in which "each of R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, C<sub>1-5</sub> alkoxy, C<sub>1-5</sub> alkylthio, halogen, or a 4-7 membered carbocyclyl or heterocyclyl; alternatively, R<sup>5</sup> and R<sup>6</sup> can be taken together to form an optionally substituted 6-membered carbocyclic ring, which ring may be unsaturated or aromatic, and may be optionally substituted with ...". The '673 Application, Amendment and Response "C", filed January 28, 2005. (A list of the presently pending claims in the '673 Application is provided in Attachment "A").

It follows from at least the quoted recitations of portions of the claims in the '673 Application and portions of the claims in the present application, that such claims recite different subject matter.

Applicants respectfully submit that the pending claims may not be rejected under the nonstatutory double patenting doctrine in view of claims of the '673 Application, and consequently request the removal of these rejections.

Andronati, reference cited in the Office Action, does not disclose the presently claimed compounds and therefore may not anticipate the presently claimed compounds. The pending claims recite, *inter alia*, compounds that comprise an entity with “R<sup>5</sup> and R<sup>6</sup> ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...”. Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. In contrast, Andronati discloses compounds for which R<sup>5</sup> and R<sup>6</sup> are taken together to form a fused phenyl ring. There are further differences and distinguishing features between the structures disclosed in Andronati and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that Andronati does not disclose the claimed subject matter and thus Andronati may not anticipate the pending claims. At least these differences in structural features also apply to the compounds disclosed in the British patent referred to in the Office Action. Consequently the British patent does not disclose the claimed subject matter and thus this reference may not anticipate the pending claims.

Andronati may not render the presently claimed compounds obvious because, in addition to not disclosing the presently claimed compounds, Andronati discloses different activity and Andronati does not teach or suggest what modifications should be made to the compounds disclosed therein to make the presently claimed compounds that in addition exhibit activity that is different from that disclosed in Andronati. In this regard, Andronati discloses indazole derivatives and reports on “the affinity of 3-aryl-[ (4-phenyl-1-piperazinyl)butyl]indazole derivatives to both 5-HT<sub>1A</sub> serotonin and D<sub>1</sub> dopamine receptors and to reveal the perspective biologically active compounds of this series.” Andronati, p. 99, col. 2.

The British patent may not render the presently claimed compounds obvious because, in addition to not disclosing the presently claimed compounds, this reference does not teach or suggest what modifications should be made to the compounds disclosed therein to make the presently claimed compounds with the presently claimed different structures.

Applicants respectfully request favorable consideration of the present Amendment and Response to place the present application in condition for allowance.

Respectfully submitted,



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Dated: January 28, 2005

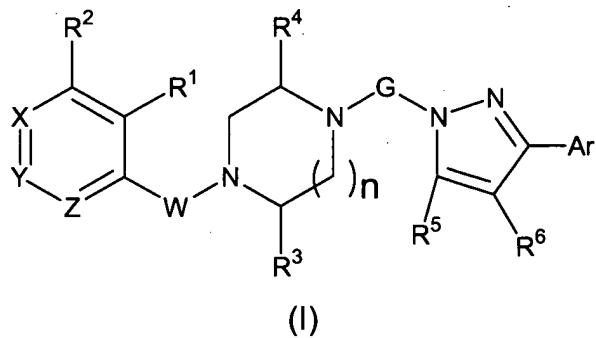
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : J. Guy Breitenbucher, *et al.* )  
Serial No. : 09/928,122 ) Art Unit  
Filed : August 10, 2001 ) 1624  
Title : Substituted pyrazoles )  
Examiner : Richard L. RAYMOND )  
Confirmation Number: 6262 )

Attachment "A" to Amendment and Response "C"

Pending claims in the '041 Application:

1. (Previously presented) A method for treating a subject with an allergic condition, said method comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising a compound of formula (I) below:



wherein:

R<sup>1</sup> is hydrogen, azido, halogen, C<sub>1-5</sub> alkoxy, hydroxy, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, cyano, nitro, R<sup>7</sup>R<sup>8</sup>N, C<sub>2-8</sub> acyl, R<sup>9</sup>OC=O, R<sup>10</sup>R<sup>11</sup>NC=O, or R<sup>10</sup>R<sup>11</sup>NSO<sub>2</sub>; or R<sup>1</sup> is taken together with W as described below;

tetrahydro-pyrazolo[4,3-c]pyridine-5-carboxylic acid amide ;  
2-(4-{3-[5-Acetyl-3-(4-iodo-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-2-hydroxy-propyl}-piperazin-1-yl)-benzonitrile ;  
2-(4-{3-[3-(4-Chloro-3-methyl-phenyl)-5-methanesulfonyl-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-2-hydroxy-propyl}-piperazin-1-yl)-benzonitrile;  
1-(3-(4-Chloro-3-methyl-phenyl)-1-{3-[4-(2,4-dimethyl-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-ethanone;  
1-{3-[4-(3,5-Dichloro-pyridin-4-yl)-piperazin-1-yl]-propyl}-5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine ;  
2-(4-{3-[5-Methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-benzonitrile;  
N-[3-Chloro-2-(4-{3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-phenyl]-methanesulfonamide ;  
3-(3,4-Dichloro-phenyl)-1-{3-[4-(2-nitro-phenyl)-piperazin-1-yl]-propyl}-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridine-5-carboxylic acid amide;  
and 3-(4-Chloro-3-methyl-phenyl)-1-{3-[4-(2-cyano-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridine-5-carboxylic acid amide.

6. (Previously presented) A method of claim 1, wherein said compound is selected from :

1-(3-(4-Chloro-phenyl)-1-{3-[4-(2-fluoro-phenyl)-piperazin-1-yl]-propyl}-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-ethanone;  
1-{3-(4-Chloro-phenyl)-1-[2-hydroxy-3-(4-o-tolyl-piperazin-1-yl)-propyl]-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl}-ethanone;  
1-{3-(4-Chloro-phenyl)-1-[2-methoxy-3-(4-o-tolyl-piperazin-1-yl)-propyl]-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl}-ethanone;

1-[1-{2-Hydroxy-3-[4-(2-hydroxy-phenyl)-piperazin-1-yl]-propyl}-3-(4-iodo-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethanone;

1-[1-[2-Hydroxy-3-(4-o-tolyl-piperazin-1-yl)-propyl]-3-(4-trifluoromethyl-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethanone;

2-(4-{3-[5-Acetyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-2-hydroxy-propyl}-piperazin-1-yl)-benzonitrile;

1-[1-[2-(2-Piperazin-1-yl-ethylamino)-3-(4-o-tolyl-piperazin-1-yl)-propyl]-3-(4-trifluoromethyl-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethanone;

1-{3-[4-(2-Cyano-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-3-(4-iodo-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridine-5-carboxylic acid tert-butyl ester;

1-{3-[4-(2-Cyano-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-3-(4-iodo-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridine-5-carboxylic acid amide;

Carbamic acid 1-[5-carbamoyl-3-(4-iodo-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-ylmethyl]-2-[4-(2-cyano-phenyl)-piperazin-1-yl]-ethyl ester;

1-{3-(3-Amino-4-chloro-phenyl)-1-[2-hydroxy-3-(4-o-tolyl-piperazin-1-yl)-propyl]-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl}-ethanone;

(R)-1-(3-(4-Bromo-phenyl)-1-{3-[4-(5-chloro-2-methyl-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-ethanone;

2-(4-{3-[5-Acetyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-2-fluoro-propyl}-piperazin-1-yl)-benzonitrile;

(3-(4-Chloro-3-methyl-phenyl)-1-{3-[4-(2-cyano-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl)-oxo-acetic acid methyl ester;

5-Methanesulfonyl-1-{3-[4-(2-nitro-phenyl)-piperazin-1-yl]-propyl}-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine;

1-[3-Chloro-2-(4-{3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-phenyl]-urea;

1-{3-[4-(2-Chloro-6-methanesulfonyl-amino-phenyl)-piperazin-1-yl]-propyl}-3-(4-trifluoromethyl-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridine-5-sulfonic acid amide;

N-[3-Chloro-2-(4-{2-hydroxy-3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-phenyl]-methanesulfonamide;

1-[4-(2,6-Dinitro-phenyl)-piperazin-1-yl]-3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propan-2-ol;

2-(4-{2-Hydroxy-3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-3-methanesulfonylamino-benzoic acid methyl ester;

1-{3-[4-(1,1-Dioxo-1H-1l6-benzo[d]isothiazol-3-yl)-piperazin-1-yl]-propyl}-5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-c]pyridine;

1-[1-{3-[4-(6-Chloro-benzothiazol-2-yl)-piperazin-1-yl]-2-hydroxy-propyl}-3-(4-trifluoromethyl-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethanone;

and

1-[1-[3-(4-Benzo[d]isoxazol-3-yl-piperazin-1-yl)-2-hydroxy-propyl]-3-(4-trifluoromethyl-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-5-yl]-ethanone.

7. (withdrawn) A method of claim 1, wherein said compound is selected from:

N-[3-Chloro-2-(4-{2-hydroxy-3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-phenyl]-methanesulfonamide;

1-[3-(4-Benzo[d]isothiazol-3-yl-piperazin-1-yl)-propyl]-3-(4-bromo-phenyl)-1,4,6,7-tetrahydro-pyrazolo[4,3-c]pyridine-5-carboxylic acid amide; and

1-[3-Chloro-2-(4-{2-hydroxy-3-[5-methanesulfonyl-3-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-pyrazolo[4,3-c]pyridin-1-yl]-propyl}-piperazin-1-yl)-phenyl]-3-methyl-urea.

8. (Previously presented) A method of claim 1, wherein said pharmaceutical composition is formulated in a dosage amount appropriate for the treatment of an allergic condition.
9. (Previously presented) A method of claim 1, wherein said condition is asthma.
10. (withdrawn) A method of claim 2, wherein said condition is asthma.
11. (withdrawn) A method of claim 3, wherein said condition is asthma.
12. (withdrawn) A method of claim 7, wherein said condition is asthma.

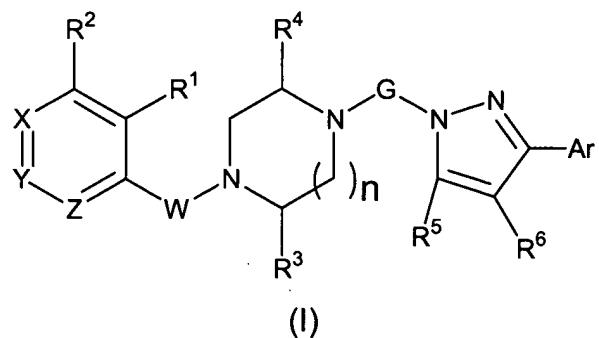
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : J. Guy Breitenbacher, *et al.* )  
Serial No. : 09/928,122 ) Art Unit  
Filed : August 10, 2001 ) 1624  
Title : Substituted pyrazoles )  
Examiner : Richard L. RAYMOND )  
Confirmation Number: 6262 )

Attachment "B" to Amendment and Response "C"

Pending claims in the '673 Application:

1. (Previously presented) A method for treating a subject with an allergic condition, said method comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising a compound of formula (I) below:



wherein:

R<sup>1</sup> is hydrogen, azido, halogen, C<sub>1-5</sub> alkoxy, hydroxy, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, cyano, nitro, R<sup>7</sup>R<sup>8</sup>N, C<sub>2-8</sub> acyl, R<sup>9</sup>OC=O, R<sup>10</sup>R<sup>11</sup>NC=O, or R<sup>10</sup>R<sup>11</sup>NSO<sub>2</sub>; or R<sup>1</sup> is taken together with W as described below;

$R^2$  is hydrogen, halogen,  $C_{1-5}$  alkoxy,  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl,  $C_{1-5}$  haloalkyl, cyano, or  $R^{48}R^{49}N$ ;  
alternatively,  $R^1$  and  $R^2$  can be taken together to form an optionally substituted 5- to 7- membered carbocyclic or heterocyclic ring, which ring may be unsaturated or aromatic;  
each of  $R^3$  and  $R^4$  is independently hydrogen or  $C_{1-5}$  alkyl;  
each of  $R^5$  and  $R^6$  is independently hydrogen,  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl,  $C_{1-5}$  alkoxy,  $C_{1-5}$  alkylthio, halogen, or a 4-7 membered carbocyclic or heterocyclic;  
alternatively,  $R^5$  and  $R^6$  can be taken together to form an optionally substituted 6- membered carbocyclic ring, which ring may be unsaturated or aromatic, and may be optionally substituted with between one and three substituents independently selected from halo, cyano, amino, nitro,  $R^{40}$ ,  $R^{40}O$ -,  $R^{40}S$ -,  $R^{40}O(C_{1-5}$  alkylene)-,  $R^{40}O(C=O)$ -,  $R^{40}(C=O)$ -,  $R^{40}(C=S)$ -,  $R^{40}(C=O)O$ -,  $R^{40}O(C=O)(C=O)$ -,  $R^{40}SO_2$ ,  $NHR^{62}(C=NH)$ -,  $NHR^{62}SO_2$ -, and  $NHR^{62}(C=O)$  -;  
 $R^{40}$  is H,  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl, phenyl, benzyl, phenethyl,  $C_{1-5}$  heterocyclic, ( $C_{1-5}$  heterocyclic) $C_{1-5}$  alkylene, amino, or mono- or di( $C_{1-5}$  alkyl)amino, or  $R^{58}OR^{59}$ -, wherein  $R^{58}$  is H,  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl, phenyl, benzyl, phenethyl,  $C_{1-5}$  heterocyclic, or ( $C_{1-5}$  heterocyclic) $C_{1-6}$  alkylene and  $R^{59}$  is  $C_{1-5}$  alkylene, phenylene, or divalent  $C_{1-5}$  heterocyclic; and  
 $R^{62}$  can be H in addition to the values for  $R^{40}$ ;  
 $R^7$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, naphthyl,  $C_{1-5}$  heterocyclic,  $C_{2-8}$  acyl, aroyl,  $R^{27}OC=O$ ,  $R^{28}R^{29}NC=O$ ,  $R^{27}SO$ ,  $R^{27}SO_2$ , or  $R^{28}R^{29}NSO_2$ ;  
 $R^8$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, or  $C_{1-5}$  heterocyclic;  
alternatively,  $R^7$  and  $R^8$  can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;  
 $R^9$  is  $C_{1-5}$  alkyl, phenyl, naphthyl, or  $C_{1-5}$  heterocyclic;  
 $R^{21}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, naphthyl,  $C_{1-5}$  heterocyclic,  $C_{2-8}$  acyl, aroyl,  $R^{30}OC=O$ ,  $R^{31}R^{32}NC=O$ ,  $R^{30}SO$ ,  $R^{30}SO_2$ , or  $R^{31}R^{32}NSO_2$ ;  
 $R^{22}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, or  $C_{1-5}$  heterocyclic;

alternatively,  $R^{21}$  and  $R^{22}$  can be taken together to form an optionally substituted 4- to 7-membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

each of  $R^{23}$ ,  $R^{26}$ ,  $R^{27}$ ,  $R^{30}$ ,  $R^{33}$ ,  $R^{44}$ ,  $R^{45}$ , and  $R^{50}$  is  $C_{1-5}$  alkyl, phenyl, naphthyl, or  $C_{1-5}$  heterocyclyl;

$R^{24}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, naphthyl,  $C_{1-5}$  heterocyclyl,  $C_{2-8}$  acyl, aroyl,  $R^{33}OC=O$ ,  $R^{34}R^{35}NC=O$ ,  $R^{33}SO$ ,  $R^{33}SO_2$ , or  $R^{34}R^{35}NSO_2$ ;

$R^{25}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, or  $C_{1-5}$  heterocyclyl;

alternatively,  $R^{24}$  and  $R^{25}$  can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

each of  $R^{10}$  and  $R^{11}$  is independently hydrogen,  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl, phenyl, or  $C_{1-5}$  heterocyclyl;

alternatively,  $R^{10}$  and  $R^{11}$  or can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

each of  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{46}$ ,  $R^{47}$ ,  $R^{51}$  and  $R^{52}$  is independently hydrogen,  $C_{1-5}$  alkyl, phenyl, or  $C_{1-5}$  heterocyclyl;

~~alternatively,  $R^{28}$  and  $R^{29}$ ,  $R^{31}$  and  $R^{32}$ ,  $R^{34}$  and  $R^{35}$ ,  $R^{46}$  and  $R^{47}$ , or  $R^{51}$  and  $R^{52}$ , independently, can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;~~

$n$  is 1;

$G$  represents  $C_{3-6}$  alkenediyl or  $C_{3-6}$  alkanediyl, optionally substituted with hydroxy, halogen,  $C_{1-5}$  alkyl,  $C_{1-5}$  alkoxy, oxo, hydroximino,  $CO_2R^{60}$ ,  $R^{60}R^{61}NCO_2$ , (L)- $C_{1-4}$  alkylene-, (L)- $C_{1-5}$  alkoxy,  $N_3$ , or [(L)- $C_{1-5}$  alkylene]amino;

each of  $R^{60}$  and  $R^{61}$  is independently hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, benzyl, phenethyl, or  $C_{1-5}$  heterocyclyl; alternatively  $R^{60}$  and  $R^{61}$ , can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

L is amino, mono- or di-C<sub>1-5</sub> alkylamino, pyrrolidinyl, morpholinyl, piperidinyl homopiperidinyl, or piperazinyl, where available ring nitrogens may be optionally substituted with C<sub>1-5</sub> alkyl, benzyl, C<sub>2-5</sub> acyl, C<sub>1-5</sub> alkylsulfonyl or C<sub>1-5</sub> alkyloxycarbonyl;

X is nitrogen or R<sup>12</sup>C;

Y is nitrogen or R<sup>13</sup>C;

Z is nitrogen or R<sup>14</sup>C;

R<sup>12</sup> is hydrogen, halogen, C<sub>1-5</sub> alkoxy, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, cyano, nitro, R<sup>21</sup>R<sup>22</sup>N, C<sub>2-8</sub> acyl, C<sub>1-5</sub> haloalkyl, C<sub>1-5</sub> heterocyclyl, (C<sub>1-5</sub> heterocyclyl)C<sub>1-5</sub> alkylene, R<sup>23</sup>OC=O, R<sup>23</sup>O(C=O)NH-, R<sup>23</sup>SO, R<sup>22</sup>NHCO-, R<sup>22</sup>NH(C=O)NH-, R<sup>23</sup>(C<sub>1-4</sub> alkylene)NHCO-, R<sup>23</sup>SO<sub>2</sub>, or R<sup>23</sup>SO<sub>2</sub>NH-;

R<sup>13</sup> is hydrogen, halogen, C<sub>1-5</sub> alkoxy, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, cyano, nitro, R<sup>42</sup>R<sup>43</sup>N, C<sub>2-8</sub> acyl, C<sub>1-5</sub> haloalkyl, C<sub>1-5</sub> heterocyclyl, (C<sub>1-5</sub> heterocyclyl)C<sub>1-5</sub> alkylene, R<sup>44</sup>OC=O, R<sup>44</sup>O(C=O)NH-, R<sup>44</sup>SO, R<sup>43</sup>NHCO-, R<sup>43</sup>NH(C=O)NH-, R<sup>44</sup>(C<sub>1-4</sub> alkylene)NHCO-, R<sup>44</sup>SO<sub>2</sub>, or R<sup>44</sup>SO<sub>2</sub>NH-;

R<sup>14</sup> is hydrogen, halogen, C<sub>1-5</sub> alkoxy, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, cyano, nitro, R<sup>24</sup>R<sup>25</sup>N, C<sub>2-8</sub> acyl, C<sub>1-5</sub> haloalkyl, C<sub>1-5</sub> heterocyclyl, (C<sub>1-5</sub> heterocyclyl)C<sub>1-5</sub> alkylene, R<sup>26</sup>OC=O, R<sup>26</sup>O(C=O)NH-, R<sup>26</sup>SO, R<sup>25</sup>NHCO-, R<sup>25</sup>NH(C=O)NH-, R<sup>26</sup>(C<sub>1-4</sub> alkylene)NHCO-, R<sup>26</sup>SO<sub>2</sub>, or R<sup>26</sup>SO<sub>2</sub>NH-; alternatively, R<sup>12</sup> and R<sup>13</sup> or R<sup>12</sup> and R<sup>2</sup> or R<sup>13</sup> and R<sup>14</sup> can be taken together to form an optionally substituted 5- to 6- membered carbocyclic or heterocyclic ring, which ring may be unsaturated or aromatic;

Ar represents a monocyclic or bicyclic aryl or heteroaryl ring, optionally substituted with between 1 and 3 substituents selected from halogen, C<sub>1-5</sub> alkoxy, C<sub>1-5</sub> alkyl, C<sub>2-5</sub> alkenyl, cyano, azido, nitro, R<sup>15</sup>R<sup>16</sup>N, R<sup>17</sup>SO<sub>2</sub>, R<sup>17</sup>S, R<sup>17</sup>SO, R<sup>17</sup>OC=O, R<sup>15</sup>R<sup>16</sup>NC=O, C<sub>1-5</sub> haloalkyl, C<sub>1-5</sub> haloalkoxy, C<sub>1-5</sub> haloalkylthio, and C<sub>1-5</sub> alkylthio;

R<sup>15</sup> is hydrogen, C<sub>1-5</sub> alkyl, C<sub>3-5</sub> alkenyl, phenyl, benzyl, C<sub>1-5</sub> heterocyclyl, C<sub>2-8</sub> acyl, aroyl, R<sup>53</sup>OC=O, R<sup>54</sup>R<sup>55</sup>NC=O, R<sup>53</sup>S, R<sup>53</sup>SO, R<sup>53</sup>SO<sub>2</sub>, or R<sup>54</sup>R<sup>55</sup>NSO<sub>2</sub>;

R<sup>16</sup> is hydrogen, C<sub>1-5</sub> alkyl, C<sub>3-5</sub> alkenyl, phenyl, benzyl, or C<sub>1-5</sub> heterocyclyl;

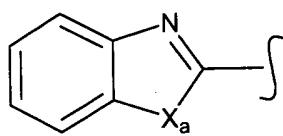
alternatively,  $R^{15}$  and  $R^{16}$  can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

each of  $R^{17}$  and  $R^{53}$  is  $C_{1-5}$  alkyl, phenyl, or  $C_{1-5}$  heterocyclyl;

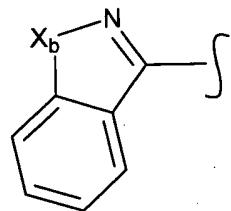
each of  $R^{54}$  and  $R^{55}$  is independently hydrogen,  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl, phenyl, benzyl, or  $C_{1-5}$  heterocyclyl;

alternatively,  $R^{54}$  and  $R^{55}$  can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

$W$  represents  $SO_2$ ,  $C=O$ ,  $CHR^{20}$ , or a covalent bond; or  $W$  and  $R^1$ , taken together with the 6-membered ring to which they are both attached, form one of the following two formulae:



(I)(a)



(I)(b)

wherein  $X_a$  is O, S, or N; and  $X_b$  is O, S or  $SO_2$ ;

$R^{20}$  is hydrogen,  $C_{1-5}$  alkyl, phenyl, benzyl, naphthyl, or  $C_{1-5}$  heterocyclyl;

$R^{42}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, naphthyl,  $C_{1-5}$  heterocyclyl,  $C_{2-8}$  acyl, aroyl,  $R^{45}OC=O$ ,  $R^{46}R^{47}NC=O$ ,  $R^{45}SO$ ,  $R^{45}SO_2$ , or  $R^{46}R^{47}NSO_2$ ;

$R^{43}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, or  $C_{1-5}$  heterocyclyl;

alternatively,  $R^{42}$  and  $R^{43}$  can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic;

$R^{44}$  is  $C_{1-5}$  alkyl,  $C_{2-5}$  alkenyl, phenyl, naphthyl, or  $C_{1-5}$  heterocyclyl;

$R^{48}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, naphthyl,  $C_{1-5}$  heterocyclyl,  $C_{2-8}$  acyl, aroyl,  $R^{50}OC=O$ ,  $R^{51}R^{52}NC=O$ ,  $R^{50}SO$ ,  $R^{50}SO_2$ , or  $R^{51}R^{52}NSO_2$ ;

$R^{49}$  is hydrogen,  $C_{1-5}$  alkyl,  $C_{3-5}$  alkenyl, phenyl, or  $C_{1-5}$  heterocyclyl;

alternatively,  $R^{48}$  and  $R^{49}$  can be taken together to form an optionally substituted 4- to 7- membered heterocyclic ring, which ring may be saturated, unsaturated or aromatic; and

wherein each of the above hydrocarbyl or heterocarbyl groups, unless otherwise indicated, and in addition to any specified substituents, is optionally and independently substituted with between 1 and 3 substituents selected from methyl, halomethyl, hydroxymethyl, halo, hydroxy, amino, nitro, cyano,  $C_{1-5}$  alkyl,  $C_{1-5}$  alkoxy,  $-COOH$ ,  $C_{2-6}$  acyl,  $[di(C_{1-4} \text{ alkyl})\text{amino}]C_{2-5}$  alkylene,  $[di(C_{1-4} \text{ alkyl})\text{amino}]C_{2-5}$  alkyl- $NH-CO-$ , and  $C_{1-5}$  haloalkoxy;

or a pharmaceutically acceptable salt, ester, or amide thereof.

2. (Previously presented) A method of claim 1, wherein each of  $R^3$  and  $R^4$  is hydrogen; Ar represents a six membered ring, optionally substituted with between 1 and 2 substituents selected from halogen,  $C_{1-5}$  alkyl, cyano, nitro,  $R^{15}R^{16}N$ ,  $CF_3$  and  $OCF_3$ ;  $R^{12}$  is hydrogen,  $R^{23}SO$ , or  $R^{23}SO_2$ ;  $R^{13}$  is hydrogen,  $R^{44}SO$ , or  $R^{44}SO_2$ ;  $R^{14}$  is hydrogen, halogen,  $C_{1-5}$  alkoxy,  $C_{1-5}$  alkyl, cyano, nitro, or  $R^{24}R^{25}N$ ; and G is  $C_3$  alkanediyl, optionally substituted with hydroxy, (L)- $C_{1-5}$  alkyloxy-, or (L)- $C_{1-5}$  alkylamino.
3. (Previously presented) A method of claim 2, wherein Ar is phenyl.
4. (Canceled)
5. (Canceled)
6. (Currently amended) A method of claim 1, wherein said compound is selected from :

1-[3-(3,4-Dichloro-phenyl)-pyrazol-1-yl]-3-(4-o-tolyl-piperazin-1-yl)-propan-2-ol.

7. (Cancelled)

8. (Previously presented) A method of claim 1, wherein said pharmaceutical composition is formulated in a dosage amount appropriate for the treatment of an allergic condition.
9. (Original) A method of claim 1, wherein said condition is asthma.
10. (Original) A method of claim 2, wherein said condition is asthma.
11. (Original) A method of claim 3, wherein said condition is asthma.
12. (Original) A method of claim 7, wherein said condition is asthma.